IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of: Peter R. Baum, William C. Fanslow III, Timothy E. Lofton, Eric A. Sorensen, and Adel Youakim

Docket No.: 3101-A

Group Art Unit: 1644

Serial No: 09/972,268

Examiner: Maher M. Haddad

Filed: October 5, 2001

For: NECTIN POLYPEPTIDES

Commissioner for Patents
Washington, D.C. 20231

RESPONSE TO RESTRICTION REQUIREMENT AND PRELIMINARY AMENDMENT

This paper is submitted in response to the Restriction Requirement dated June 18, 2002 (Paper 7, the "Office Action").

Restriction/Election

Applicants elect group III, claims 1-11 and 19 drawn to the Nectin-3 polypeptide of SEQ ID NO:6, with traverse as discussed below. Non-elected claims 12-18 and 20-53 have been canceled. Claims 54-58, consistent with this election, have been added.

In accordance with the election of species stated at page 46 of the Office Action, Applicants elect the species of claim 6(a) as that claim has been amended to read, to which claims would be restricted *if* no generic claim is finally held to be allowable. Claims 1-6, 9-11, 19, and new claims 54-58 read upon the elected species of claim 6(a).

Applicants have elected group III. Although the Office Action stated at page 46 that these groups I-VI and VIII are different products, **in fact the Nectin-3 polypeptides of SEQ ID NOs 2, 4, 6, 8, 10, 12, and 31 (corresponding to groups I-VI and VIII) are essentially identical throughout the portion of these polypeptides to which the pending claims are directed**, i.e. polypeptides comprising extracellular, nectin-1-binding, sequences of Nectin-3 polypeptides. The specification states at page 4, lines 38-39:

> Nectin-3α, β, and γ are related to each other as the products of alternative splicing: the N-terminal 356 amino acids of the full-length amino acid sequences of these polypeptides are identical.

SEQ ID NOs 2, 4, and 6 (Nectin-3α), 8, 10, and 12 (Nectin-3β), and 31 (Nectin-3γ) are all identical throughout their N-terminal 356 amino acids as shown by the alignment presented

below, except for some minor differences within the first seven amino acids at the N-terminus. Because these polypeptides contain a signal sequence which is cleaved off at a position following amino acid 50 (see the specification at page 4, line 39 through page 5, line 5), the N-terminal region containing the slight differences between SEQ ID NOs 2, 4, 6, 8, 10, 12, and 31 (amino acids 1-7) is not predicted to be present in mature Nectin-3 polypeptides.

Therefore, a claim which recites "amino acids 58 through 152 of SEQ ID NO:4, 6, 10, 12, or 31" is referring to a *single* amino acid sequence, because as can be seen from the alignment below, amino acids 58 through 152 of SEQ ID NO:4 are *identical* to amino acids 58 through 152 of SEQ ID NO:6, and are *identical* to amino acids 58 through 152 of SEQ ID NO:10, etc. Because of the identity or near-identity of the amino acid sequences to which the claims as amended are directed, searching and examining the amino acid sequences corresponding to Groups I-VI and VIII would ***not*** be unduly burdensome to the Examiner.

For at least the above reasons, Applicants respectfully traverse the restriction between Groups I-VI and VIII and request reconsideration and withdrawal of the restriction requirement with respect to groups I-VI and III.

Alignment of SEQ ID NOs 2, 4, 6, 8, 10, 12, and 31:

```
                1                                                   50
NO2   NEC3ALPHA ~~~~~~~SPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
NO4   NEC3ALPHA MARTpgPSPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
NO6   NEC3ALPHA MARTlrPSPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
NO8   NEC3BETA  ~~~~~~PSPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
NO10  NEC3BETA  MARTpgPSPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
NO12  NEC3BETA  MARTlrPSPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
NO31  NEC3GAMMA MARTlrPSPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS
      Consensus -------SPL CPGGGKAQLS SASLLGAGLL LQPPTPPPLL LLLFPLLLFS

                51                                                  100
NO2   NEC3ALPHA RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
NO4   NEC3ALPHA RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
NO6   NEC3ALPHA RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
NO8   NEC3BETA  RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
NO10  NEC3BETA  RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
NO12  NEC3BETA  RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
NO31  NEC3GAMMA RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ
      Consensus RLCGALAGPI IVEPHVTAVW GKNVSLKCLI EVNETITQIS WEKIHGKSSQ

                101                                                 150
NO2   NEC3ALPHA TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
NO4   NEC3ALPHA TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
NO6   NEC3ALPHA TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
NO8   NEC3BETA  TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
NO10  NEC3BETA  TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
NO12  NEC3BETA  TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
NO31  NEC3GAMMA TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA
      Consensus TVAVHHPQYG FSVQGEYQGR VLFKNYSLND ATITLHNIGF SDSGKYICKA

                151                                                 200
NO2   NEC3ALPHA VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
NO4   NEC3ALPHA VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
NO6   NEC3ALPHA VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
NO8   NEC3BETA  VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
NO10  NEC3BETA  VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
```

```
NO12  NEC3BETA   VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
NO31  NEC3GAMMA  VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP
      Consensus  VTFPLGNAQS STTVTVLVEP TVSLIKGPDS LIDGGNETVA AICIAATGKP

                 201                                                 250
NO2   NEC3ALPHA  VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
NO4   NEC3ALPHA  VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
NO6   NEC3ALPHA  VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
NO8   NEC3BETA   VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
NO10  NEC3BETA   VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
NO12  NEC3BETA   VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
NO31  NEC3GAMMA  VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH
      Consensus  VAHIDWEGDL GEMESTTTSF PNETATIISQ YKLFPTRFAR GRRITCVVKH

                 251                                                 300
NO2   NEC3ALPHA  PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
NO4   NEC3ALPHA  PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
NO6   NEC3ALPHA  PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
NO8   NEC3BETA   PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
NO10  NEC3BETA   PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
NO12  NEC3BETA   PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
NO31  NEC3GAMMA  PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF
      Consensus  PALEKDIRYS FILDIQYAPE VSVTGYDGNW FVGRKGVNLK CNADANPPPF

                 301                                                 350
NO2   NEC3ALPHA  KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
NO4   NEC3ALPHA  KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
NO6   NEC3ALPHA  KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
NO8   NEC3BETA   KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
NO10  NEC3BETA   KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
NO12  NEC3BETA   KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
NO31  NEC3GAMMA  KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ
      Consensus  KSVWSRLDGQ WPDGLLASDN TLHFVHPLTF NYSGVYICKV TNSLGQRSDQ

                 351                                                 400
NO2   NEC3ALPHA  KVIYISDpPt ttTlqptiqw hpStadiedl atepkklpFp lstlaTikdd
NO4   NEC3ALPHA  KVIYISDpPt ttTlqptiqw hpStadiedl atepkklpFp lstlaTikdd
NO6   NEC3ALPHA  KVIYISDpPt ttTlqptiqw hpStadiedl atepkklpFp lstlaTikdd
NO8   NEC3BETA   KVIYISDVPF KQT.......  ..SSIAVAGA VIGAVLALFI IAIFVTVL.L
NO10  NEC3BETA   KVIYISDVPF KQT.......  ..SSIAVAGA VIGAVLALFI IAIFVTVL.L
NO12  NEC3BETA   KVIYISDVPF KQT.......  ..SSIAVAGA VIGAVLALFI IAIFVTVL.L
NO31  NEC3GAMMA  KVIYISDVPF KQT.......  ..SSIAVAGA VIGAVLALFI IAIFVTVL.L
      Consensus  KVIYISD---  ----------  ----------  ----------  ----------

                 401                                                 450
NO2   NEC3ALPHA  TiatiiaSvv ggalfivlvs vlagifcyRr rrtfrgDyF.  ..aknYiPps
NO4   NEC3ALPHA  TiatiiaSvv ggalfivlvs vlagifcyRr rrtfrgDyF.  ..aknYiPps
NO6   NEC3ALPHA  TiatiiaSvv ggalfivlvs vlagifcyRr rrtfrgDyF.  ..aknYiPps
NO8   NEC3BETA   TPRKKRPSYL DKVIDLPPTH KPPPLYEERS PPLPQKDLFQ  ...pEhlPlq
NO10  NEC3BETA   TPRKKRPSYL DKVIDLPPTH KPPPLYEERS PPLPQKDLFQ  ...pEhlPlq
NO12  NEC3BETA   TPRKKRPSYL DKVIDLPPTH KPPPLYEERS PPLPQKDLFQ  ...pEhlPlq
NO31  NEC3GAMMA  TPRKKRPSYL DKVIDLPPTH KPPPLYEERS PPLPQKDLFQ  vcvhEYt~~~

                 451                                                 500
NO2   NEC3ALPHA  dmqKEsqidv LQqde.LdSy pdsvkkENkn pvnnlirkdy LeepektQwn
NO4   NEC3ALPHA  dmqKEsqidv LQqde.LdSy pdsvkkENkn pvnnlirkdy LeepektQwn
NO6   NEC3ALPHA  dmqKEsqidv LQqde.LdSy pdsvkkENkn pvnnlirkdy LeepektQwn
NO8   NEC3BETA   tqfKErevgn LQhsngLnSr sfdyedENpv gedgiqqmyp LynqmcyQdr
NO10  NEC3BETA   tqfKErevgn LQhsngLnSr sfdyedENpv gedgiqqmyp LynqmcyQdr
NO12  NEC3BETA   tqfKErevgn LQhsngLnSr sfdyedENpv gedgiqqmyp LynqmcyQdr

                 501                                                 553
NO2   NEC3ALPHA  nvenlnrfer PmdyYeDlkm gmkfvsdehy deneddlvsh vdgsvisrre wyv
NO4   NEC3ALPHA  nvenlnrfer PmdyYeDlkm gmkfvsdehy deneddlvsh vdgsvisrre wyv
NO6   NEC3ALPHA  nvenlnrfer PmdyYeDlkm gmkfvsdehy deneddlvsh vdgsvisrre wyv
NO8   NEC3BETA   spgkhhqnnd PkrvYiDpre hyv~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~
NO10  NEC3BETA   spgkhhqnnd PkrvYiDpre hyv~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~
NO12  NEC3BETA   spgkhhqnnd PkrvYiDpre hyv~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~
```

Preliminary Amendment

Please enter the following amendments before examining this application.

In the Title

Please amend the title as shown in the rewritten version that follows:

NECTIN POLYPEPTIDES

In the Claims

Please cancel non-elected claims 12-18 and 20-53 without prejudice to present such claims in subsequent applications.

Please amend claims 1-6, 8-9, and 19 as shown in the rewritten version that follows:

---

1 (amended). A substantially purified polypeptide comprising an amino acid sequence that is at least 80% identical to at least 20 contiguous amino acids of a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1.

2 (amended). The substantially purified polypeptide of claim 1, comprising an amino acid sequence that is at least 90% identical to at least 20 contiguous amino acids of a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1.

A1

3 (amended). The substantially purified polypeptide of claim 1, comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:2, 4, 6, 8, 10, 12, and 31; and

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1.

4 (amended). A substantially purified soluble polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence that is at least 80% identical to at least 20 contiguous amino acids of the extracellular domain of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1; and

from about x_1 to 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 404 of SEQ ID NO:4 or 6;

from about amino acid 74 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 404 of SEQ ID NO:4 or 6;

from about x_1 to 365 of SEQ ID NO:10, 12, or 31 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 365 of SEQ ID NO:10, 12, or 31; and

from about amino acid 74 to 365 of SEQ ID NO:10, 12, or 31;

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1; and

(c) a fragment of an amino acid sequence of (a) that inhibits endothelial cell migration;

and X is a peptide linker.

A1 Cont'd

9 (amended). The soluble polypeptide of claim 4, wherein the polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:13, 14, 15, and 16.

A2

19 (amended). A polypeptide of claim 4 produced by culturing a recombinant host cell genetically engineered to contain a polynucleotide encoding the polypeptide of claim 4 under conditions promoting expression of said polypeptide.

Please add new claims 54-58 as shown below:

A3

54 (NEW). The polypeptide of claim 19, wherein the polypeptide is produced by a method further comprising substantially purifying said polypeptide.

55 (NEW). A substantially purified polypeptide comprising amino acids 74 through 152 of SEQ ID NO:4, 6, 10, 12, or 31.

(b) an amino acid sequence of (a) that inhibits endothelial cell migration.

5 (amended). The substantially purified soluble polypeptide of claim 4, comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence that is at least 90% identical to at least 20 contiguous amino acids of the extracellular domain of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1; and

(b) an amino acid sequence of (a) that inhibits endothelial cell migration.

6 (amended). The substantially purified polypeptide of claim 4, comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence selected from the group consisting of:

from about x_1 to 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 404 of SEQ ID NO:4 or 6;

from about amino acid 74 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 404 of SEQ ID NO:4 or 6;

from about x_1 to 365 of SEQ ID NO:10, 12, or 31 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 365 of SEQ ID NO:10, 12, or 31; and

from about amino acid 74 to 365 of SEQ ID NO:10, 12, or 31;

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1; and

(c) a fragment of an amino acid sequence of (a) that inhibits endothelial cell migration.

8 (amended). The soluble polypeptide according to claim 7, comprising a sequence Z_1-X-Z_2, wherein Z_1 and Z_2 are each individually an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence selected from the group consisting of:

56 (NEW). A substantially purified polypeptide that binds nectin-1 and comprises an amino acid sequence that is at least 80% identical to amino acids 74 through 152 of SEQ ID NO:4, 6, 10, 12, or 31.

57 (NEW). A polypeptide produced by culturing a recombinant host cell genetically engineered to contain a polynucleotide encoding said polypeptide under conditions promoting expression of said polypeptide, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of:

(a) amino acids x_1 through 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39;

amino acids 58 through 152 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 58 through 250 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 58 through 342 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 58 through 404 of SEQ ID NO:4 or 6;

amino acids 74 through 152 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 74 through 250 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 74 through 342 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 74 through 404 of SEQ ID NO:4 or 6;

amino acids x_1 through 365 of SEQ ID NO:10, 12, or 31 wherein x_1 is an amino acid between 1 and 39;

amino acids 58 through 365 of SEQ ID NO:10, 12, or 31; and

amino acids 74 through 365 of SEQ ID NO:10, 12, or 31;

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1; and

(c) a fragment of an amino acid sequence of (a) that inhibits endothelial cell migration.

58 (NEW). The polypeptide of claim 57, wherein the polypeptide is produced by a method further comprising substantially purifying said polypeptide.

REMARKS

The title has been amended to more accurately reflect the elected subject matter. Claims 1-6, 8-9, and 19 have been amended to remove non-elected subject matter, and new claims 54-58 have been added. Support for the amendments to the claims and for the added

claims is found throughout the specification and the claims as filed, as for example at page 15, line 35; no new matter has been added. A marked-up copy of the amended claims 1-6, 8-9, and 19 showing changes made is presented as Appendix A; a rewritten version of the entire set of pending claims is presented as Appendix B.

Supplemental Information Disclosure Statement

The Examiner is requested to note that a Supplemental Information Disclosure Statement and accompanying form PTO-1449 are being filed herewith.

If a telephone interview would be helpful in advancing the prosecution of this application, Applicants' attorney invites the Examiner to contact her at the number provided below.

Respectfully submitted,

Immunex Corporation
Law Department
51 University Street
Seattle, WA 98101

Suzanne A. Sprunger, Ph.D.
Attorney for Applicants
Registration No. 41,323
Telephone (206) 265-4071

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents; Washington, D.C. 20231, on the date indicated below.

Date: October 17, 2002 Signed: _____
Kathleen F. Prindle

Appendix A
U.S. Serial No. 09/972,268
Marked-Up Version to Show Changes Made

The title has been amended:

NECTIN POLYPEPTIDES[, POLYNUCLEOTIDES, METHODS OF MAKING AND USE THEREOF]

Claims 1-6, 8-9, and 19 are amended:

1 (amended). A substantially purified polypeptide comprising an amino acid sequence [selected from the group consisting of:]

[(a) a polypeptide comprising a sequence]that is at least 80% identical to at least 20 contiguous amino acids of a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, [24,]and 31[, 34, and 37-39], wherein [the]a polypeptide consisting of said amino acid sequence binds to nectin-1[; and]

[(b) a fragment of (a) that binds to nectin-1].

2 (amended). The substantially purified polypeptide of claim 1, [wherein the polypeptide is]comprising an amino acid sequence [selected from the group consisting of:]

[(a) a polypeptide comprising a sequence]that is at least 90% identical to at least 20 contiguous amino acids of a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, [24,]and 31[, 34, and 37-39], wherein [the]a polypeptide consisting of said amino acid sequence binds to nectin-1[; and]

[(b) a fragment of (a) that binds to nectin-1].

3 (amended). The substantially purified polypeptide of claim 1, [wherein the polypeptide is]comprising an amino acid sequence selected from the group consisting of:

(a) [a polypeptide comprising a sequence selected from the group consisting of]SEQ ID NO:2, 4, 6, 8, 10, 12, [24,]and 31[, 34, and 37-39]; and

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1.

4 (amended). A substantially purified soluble polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) [a polypeptide comprising a]an amino acid sequence that is at least 80% identical to at least 20 contiguous amino acids of the extracellular domain of SEQ ID NO:2, 4, 6, 8, 10, 12, [24,]and 31[, 34, and 37-39], wherein [the]a polypeptide consisting of said amino acid sequence binds to nectin-1;

[(b) a fragment of (a) that binds to nectin-1;] and

([c]b) [a fragment]an amino acid sequence of (a) that inhibits endothelial cell migration.

5 (amended). The substantially purified soluble polypeptide of claim 4, [wherein the polypeptide is]comprising an amino acid sequence selected from the group consisting of:

(a) [a polypeptide comprising a]an amino acid sequence that is at least 90% identical to at least 20 contiguous amino acids of the extracellular domain of SEQ ID NO:2, 4, 6, 8, 10, 12, [24,]and 31[, 34, and 37-39], wherein [the]a polypeptide consisting of said amino acid sequence binds to nectin-1;

[(b) a fragment of (a) that binds to nectin-1;] and

([c]b) [a fragment]an amino acid sequence of (a) that inhibits endothelial cell migration.

6 (amended). The substantially purified polypeptide of claim 4, [wherein the polypeptide is]comprising an amino acid sequence selected from the group consisting of:

(a) [a polypeptide comprising a]an amino acid sequence selected from the group consisting of:

from about x_1 to 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39[,];

from about amino acid 58 to 152 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 58 to 250 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 58 to 342 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 58 to 404 of SEQ ID NO:4 or 6[,];

from about amino acid 74 to 152 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 74 to 250 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 74 to 342 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 74 to 404 of SEQ ID NO:4 or 6[,];

[from about amino acid 189 to 250 of SEQ ID NO:4 or 6, from about amino acid 189 to 342 of SEQ ID NO:4 or 6, from about amino acid 189 to 404 of SEQ ID NO:4 or 6, from about amino acid 287 to 342 of SEQ ID NO:4 or 6, and from about amino acid 287 to 404 of SEQ ID NO:4 or 6;]

[(b) a polypeptide comprising a sequence selected from the group consisting of:] from about x_1 to 365 of SEQ ID NO:10, 12, or [12]31 wherein x_1 is an amino acid between 1 and 39[,];

[from about amino acid 58 to 152 of SEQ ID NO:10 or 12, from about amino acid 58 to 250 of SEQ ID NO:10 or 12, from about amino acid 58 to 342 of SEQ ID NO:10 or 12,] from about amino acid 58 to 365 of SEQ ID NO:10, 12, or [12]31[,]; and

[from about amino acid 74 to 152 of SEQ ID NO:10 or 12, from about amino acid 74 to 250 of SEQ ID NO:10 or 12, from about amino acid 74 to 342 of SEQ ID NO:10 or 12,] from about amino acid 74 to 365 of SEQ ID NO:10, 12, or [12]31[,];

[from about amino acid 189 to 250 of SEQ ID NO:10 or 12, from about amino acid 189 to 342 of SEQ ID NO:10 or 12, from about amino acid 189 to 365 of SEQ ID NO:10 or 12, from about amino acid 287 to 342 of SEQ ID NO:10 or 12, and from about amino acid 287 to 365 of SEQ ID NO:10 or 12;]

[(c) a polypeptide comprising a sequence selected from the group consisting of from about x_2 to 349 of SEQ ID NO:24 or 34 wherein x_2 is an amino acid between 1 and 16, from about amino acid 27 to 350 of SEQ ID NO:36, from about amino acid 44 to 362 of SEQ ID NO:37, from about amino acid 39 to 242 of SEQ ID NO:38, and from about amino acid 44 to 363 of SEQ ID NO:39;]

([d]b) a fragment of an amino acid sequence of (a)[, (b), or (c)] that binds to nectin-1; and

([e]c) a fragment of an amino acid sequence of (a)[, (b), or (c)] that inhibits endothelial cell migration.

8 (amended). The soluble polypeptide according to claim 7, comprising a sequence Z_1-X-Z_2, wherein Z_1 and Z_2 are each individually [a soluble polypeptide]an amino acid sequence selected from the group consisting of:

(a) [a polypeptide comprising a]an amino acid sequence selected from the group consisting of:

from about x_1 to 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39[,];

from about amino acid 58 to 152 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 58 to 250 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 58 to 342 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 58 to 404 of SEQ ID NO:4 or 6[,];

from about amino acid 74 to 152 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 74 to 250 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 74 to 342 of SEQ ID NO:4, 6, 10, 12, or 31[6,];

from about amino acid 74 to 404 of SEQ ID NO:4 or 6[,];

[from about amino acid 189 to 250 of SEQ ID NO:4 or 6, from about amino acid 189 to 342 of SEQ ID NO:4 or 6, from about amino acid 189 to 404 of SEQ ID NO:4 or 6, from about amino acid 287 to 342 of SEQ ID NO:4 or 6, and from about amino acid 287 to 404 of SEQ ID NO:4 or 6;]

[(b) a polypeptide comprising a sequence selected from the group consisting of:] from about x_1 to 365 of SEQ ID NO:10, 12, or [12]31 wherein x_1 is an amino acid between 1 and 39[,];

[from about amino acid 58 to 152 of SEQ ID NO:10 or 12, from about amino acid 58 to 250 of SEQ ID NO:10 or 12, from about amino acid 58 to 342 of SEQ ID NO:10 or 12,] from about amino acid 58 to 365 of SEQ ID NO:10, 12, or [12]31[,]; and

[from about amino acid 74 to 152 of SEQ ID NO:10 or 12, from about amino acid 74 to 250 of SEQ ID NO:10 or 12, from about amino acid 74 to 342 of SEQ ID NO:10 or 12,] from about amino acid 74 to 365 of SEQ ID NO:10, 12, or [12]31[,];

[from about amino acid 189 to 250 of SEQ ID NO:10 or 12, from about amino acid 189 to 342 of SEQ ID NO:10 or 12, from about amino acid 189 to 365 of SEQ ID NO:10 or 12, from about amino acid 287 to 342 of SEQ ID NO:10 or 12, and from about amino acid 287 to 365 of SEQ ID NO:10 or 12;]

[(c) a polypeptide comprising a sequence selected from the group consisting of from about x_2 to 349 of SEQ ID NO:24 or 34 wherein x_2 is an amino acid between 1 and 16, from about amino acid 27 to 350 of SEQ ID NO:36, from about amino acid 44 to 362 of SEQ ID NO:37, from about amino acid 39 to 242 of SEQ ID NO:38, and from about amino acid 44 to 363 of SEQ ID NO:39;]

([d]b) a fragment of an amino acid sequence of (a)[, (b), or (c)] that binds to nectin-1; and

([e]c) a fragment of an amino acid sequence of (a)[, (b), or (c)] that inhibits endothelial cell migration[,];

and X is a peptide linker.

9 (amended). The soluble polypeptide of claim 4, wherein the polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:13, 14, 15, and 16[, and 36].

19 (amended). A polypeptide of claim 4 produced by culturing [the]a recombinant host cell [of claim 17]genetically engineered to contain a polynucleotide encoding the polypeptide of claim 4 under conditions [to]promot[e]ing expression of [the]said polypeptide.

Appendix B

U.S. Serial No. 09/972,268

Rewritten Version of Pending Claims as of October 2002

Claims 12-18 and 20-53: Canceled.

Claims 1-6, 8-9, and 19: Amended.

Claims 54-58: Added.

1 (amended). A substantially purified polypeptide comprising an amino acid sequence that is at least 80% identical to at least 20 contiguous amino acids of a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1.

2 (amended). The substantially purified polypeptide of claim 1, comprising an amino acid sequence that is at least 90% identical to at least 20 contiguous amino acids of a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1.

3 (amended). The substantially purified polypeptide of claim 1, comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:2, 4, 6, 8, 10, 12, and 31; and

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1.

4 (amended). A substantially purified soluble polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence that is at least 80% identical to at least 20 contiguous amino acids of the extracellular domain of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1; and

(b) an amino acid sequence of (a) that inhibits endothelial cell migration.

5 (amended). The substantially purified soluble polypeptide of claim 4, comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence that is at least 90% identical to at least 20 contiguous amino acids of the extracellular domain of SEQ ID NO:2, 4, 6, 8, 10, 12, and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1; and

(b) an amino acid sequence of (a) that inhibits endothelial cell migration.

6 (amended). The substantially purified polypeptide of claim 4, comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence selected from the group consisting of:

from about x_1 to 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 404 of SEQ ID NO:4 or 6;

from about amino acid 74 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 404 of SEQ ID NO:4 or 6;

from about x_1 to 365 of SEQ ID NO:10, 12, or 31 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 365 of SEQ ID NO:10, 12, or 31; and

from about amino acid 74 to 365 of SEQ ID NO:10, 12, or 31;

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1; and

(c) a fragment of an amino acid sequence of (a) that inhibits endothelial cell migration.

7. A soluble polypeptide according to claim 4, further comprising a leucine zipper polypeptide, an Fc polypeptide, or a peptide linker.

8 (amended). The soluble polypeptide according to claim 7, comprising a sequence Z_1-X-Z_2, wherein Z_1 and Z_2 are each individually an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence selected from the group consisting of:

from about x_1 to 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 58 to 404 of SEQ ID NO:4 or 6;

from about amino acid 74 to 152 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 250 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 342 of SEQ ID NO:4, 6, 10, 12, or 31;

from about amino acid 74 to 404 of SEQ ID NO:4 or 6;

from about x_1 to 365 of SEQ ID NO:10, 12, or 31 wherein x_1 is an amino acid between 1 and 39;

from about amino acid 58 to 365 of SEQ ID NO:10, 12, or 31; and

from about amino acid 74 to 365 of SEQ ID NO:10, 12, or 31;

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1; and

(c) a fragment of an amino acid sequence of (a) that inhibits endothelial cell migration;

and X is a peptide linker.

9 (amended). The soluble polypeptide of claim 4, wherein the polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:13, 14, 15, and 16.

10. A composition comprising a polypeptide of claim 1 and a pharmaceutically acceptable carrier.

11. A composition comprising a polypeptide of claim 4 and a pharmaceutically acceptable carrier.

19 (amended). A polypeptide of claim 4 produced by culturing a recombinant host cell genetically engineered to contain a polynucleotide encoding the polypeptide of claim 4 under conditions promoting expression of said polypeptide.

54 (NEW). The polypeptide of claim 19, wherein the polypeptide is produced by a method further comprising substantially purifying said polypeptide.

55 (NEW). A substantially purified polypeptide comprising amino acids 74 through 152 of SEQ ID NO:4, 6, 10, 12, or 31.

56 (NEW). A substantially purified polypeptide that binds nectin-1 and comprises an amino acid sequence that is at least 80% identical to amino acids 74 through 152 of SEQ ID NO:4, 6, 10, 12, or 31.

57 (NEW). A polypeptide produced by culturing a recombinant host cell genetically engineered to contain a polynucleotide encoding said polypeptide under conditions promoting expression of said polypeptide, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of:

(a) amino acids x_1 through 404 of SEQ ID NO:4 or 6 wherein x_1 is an amino acid between 1 and 39;

amino acids 58 through 152 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 58 through 250 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 58 through 342 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 58 through 404 of SEQ ID NO:4 or 6;

amino acids 74 through 152 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 74 through 250 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 74 through 342 of SEQ ID NO:4, 6, 10, 12, or 31;

amino acids 74 through 404 of SEQ ID NO:4 or 6;

amino acids x_1 through 365 of SEQ ID NO:10, 12, or 31 wherein x_1 is an amino acid between 1 and 39;

amino acids 58 through 365 of SEQ ID NO:10, 12, or 31; and

amino acids 74 through 365 of SEQ ID NO:10, 12, or 31;

(b) a fragment of an amino acid sequence of (a) that binds to nectin-1; and

(c) a fragment of an amino acid sequence of (a) that inhibits endothelial cell migration.

58 (NEW). The polypeptide of claim 57, wherein the polypeptide is produced by a method further comprising substantially purifying said polypeptide.